

CLAIMS

Sub 1 1. A method of enhancing the efficiency of delivery of a nucleic acid to a cell, said method comprising

- a) providing to said cell an agent capable of enhancing the cytoskeletal permissiveness of said cell for transfection in an amount effective to enhance said cytoskeletal permissiveness; and
- b) providing to said cell a nucleic acid delivery system for the transfection of said cell, whereby the efficiency of delivery of a nucleic acid to said cell is enhanced.

2. The method of claim 1, wherein said agent is an isolated nucleic acid encoding a protein or a polypeptide, wherein said protein or said polypeptide when expressed in said cell is capable of enhancing the cytoskeletal permissiveness of said cell for transfection.

Sub 2 3. The method of claim 1, wherein said nucleic acid delivery system is provided to said cell simultaneously with providing said agent.

4. The method of claim 1, wherein said nucleic acid delivery system is provided to said cell prior to providing said agent.

5. The method of claim 1, wherein said nucleic acid delivery system is provided to said cell after providing said agent.

6. The method of claim 1, wherein said agent is denatured collagen or a peptide thereof.

7. The method of claim 1, wherein said agent is Thymosin beta-4 (TB4) or a peptide thereof.

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8. The method of claim 1, wherein said agent is Tenascin C or a peptide thereof.

9. The method of claim 1, wherein said agent comprises Tenascin C and TB4.

10. The method of claim 2, wherein said protein is one or more of Tenascin C, TB4 and peptides thereof.

11. The method of claim 2, wherein said isolated nucleic acid is provided to said cell using a vector selected from the group consisting of a plasmid vector, a viral vector, and a linearized nucleic acid.

12. The method of claim 1, wherein said nucleic acid delivery system comprises a vector selected from the group consisting of a plasmid vector, a viral vector, and a linearized nucleic acid.

13. The method of claim 1, wherein enhancing said cytoskeletal permissiveness for transfection comprises inhibiting DNAase I activity in the milieu surrounding or the cytoplasm of said cell.

14. The method of claim 1, wherein enhancing said cytoskeletal permissiveness for transfection comprises reducing the overall electronegative charge of the milieu surrounding or the cytoplasm of said cell to be transfected.

15. The method of claim 14, wherein enhancing said cytoskeletal permissiveness comprises enhancing the level of G-Actin in said cell.

16. The method of claim 15, wherein enhancing said level of G-Actin comprises depolymerizing F-Actin to G-Actin.

17. The method of claim 1, wherein said agent is a compound capable of modulating an ion channel in said cell.

18. ~~The method of claim 1, wherein said agent is an actin binding protein~~

19. The method of claim 1, wherein said agent is a compound capable of rendering G-Actin less susceptible to proteolysis upon binding with G-Actin.

20. The method of claim 19, wherein said compound is selected from the group consisting of beryllium fluoride and a cadmium salt.

21. The method of claim 15, wherein said level of G-Actin is enhanced by directly or indirectly upregulating TB4.

22. The method of claim 21, wherein said TB4 is indirectly upregulated by growing said cell on a Tenascin C inducing substrate.

23. The method of claim 22, wherein said Tenascin C inducing substrate is denatured collagen or a peptide thereof.

24. The method of claim 1, wherein said agent is a modulator of an intermediate in the Tenascin C and TB4 receptor-signaling pathway.

25. The method of claim 1, wherein said agent is a cytochalasin.

26. The method of claim 1, wherein said agent is selected from the group consisting of a TB4 promoter, a molecule which participates in cell-cell interactions, a molecule which participates in cell-cell adhesion, and a synthetic

extracellular matrix molecule having design features effective to enhance the cytoskeletal permissiveness of a cell for transfection.

Supp 3 27. A composition for enhancing the efficiency of delivery of a nucleic acid to a cell, said composition comprising

- a) an agent capable of enhancing the cytoskeletal permissiveness of said cell for transfection in an amount effective to enhance said permissiveness; and
- b) a nucleic acid delivery system for the transfection of said cell.

28. The composition of claim 27, wherein said nucleic acid delivery system is selected from the group consisting of a plasmid vector, a viral vector, and a linearized nucleic acid.

29. The composition of claim 27, wherein said agent is an isolated nucleic acid encoding a protein or a polypeptide, wherein said protein or said polypeptide when expressed in said cell is capable of enhancing the cytoskeletal permissiveness of said cell for transfection.

30. The composition of claim 29, wherein said isolated nucleic acid is a component of a nucleic acid delivery system.

31. The composition of claim 29, wherein said polypeptide is selected from the group consisting of TB4, Tenascin C and peptides thereof.

32. The composition of claim 27, wherein said agent is selected from the group consisting of TB4 or a peptide thereof, Tenascin C or a peptide thereof, an actin depolymerization agent, a cytochalasin, a modulator of TB4, a modulator of an intermediate in the Tenascin C and TB4 receptor-signaling pathway, a nuclease inhibitor and denatured collagen or a peptide thereof.

33. A kit for enhancing the efficiency of delivery of a nucleic acid to a cell, said kit comprising

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- 35 -